

Remarks

Applicant appreciates the thorough examination of the present application as evidenced by the Office Action dated April 21, 2006. Claims 23 and 26-51 are pending in the present application upon entry of the present Amendment. Applicant respectfully submits that Claims 23 and 26-51 are patentable for at least the reasons presented below.

I. Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 30 and 31 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. *See* Office Action, page 2. In order to address this rejection, Applicant has amended Claims 30 and 31 to recite "the body cavity." Accordingly, Applicants respectfully submit that this rejection has been obviated, and Applicant respectfully requests that this rejection be withdrawn.

II. Claim Rejections Under 35 U.S.C. § 103

Claims 23 and 26-35 stand rejected under 35 U.S.C. § 103(a) as being obvious over Dobbie, "Separation of Peritoneal Surfaces Through the Maintenance of an Artificial Ascites as a Preventative of Peritoneal Adhesions". Abstract, 4th Peritoneum and Peritoneal Access Meeting, September 16-19, 1997 (hereinafter, "the Dobbie abstract") in view of U.S. Patent No. 4,886,789 to Milner (hereinafter, "Milner"). *See* Office Action, pages 2-3. More specifically, the Office Action states the following:

One of ordinary skill would be motivated to combine the teachings of the Dobbie reference with the Milner patent since both references disclose the application of a dextrin solution to the peritoneal cavity.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the dextrin used to reduce the incidence of adhesion in a body cavity of the Dobbie reference with dextrin having 15% polymers with a degree of polymerization greater than 12 in view of the recognition in the art, as evidenced by the Milner patent

Office Action, page 4. Applicant respectfully disagrees.

In order to distinguish the present invention from the processes discussed in the cited references, it is important to first discuss the process of peritoneal dialysis.

Peritoneal Dialysis

In kidney disease, the kidneys are irreversibly damaged by disease and can no longer effectively fulfil their role of filtering and removing wastes, toxins and fluids from the body. In the peritoneal dialysis treatment-approach, these extra wastes, toxins and fluids are removed from the blood inside the body by using the body's own peritoneal membrane, or abdominal lining, as a natural filter. Peritoneal dialysis is a home- as opposed to hospital-based treatment. Dialysis fluids are introduced into the peritoneal cavity through a permanently surgically implanted flexible catheter in the abdomen. Extra fluid and waste may travel across the peritoneal membrane into the dialysis fluid, which is then **drained** from the abdomen through the catheter **after a pre-determined in-dwelling period**. A new volume of solution is then instilled and the treatment technique repeated. This process is discussed in Milner at column 1, lines 15-41 and is further described in more detail below.

A person performing peritoneal dialysis typically will undergo **at least four exchanges per day**, one of which is named the "long dwell" exchange. The "dwell" is the *length of time the dialysis solution remains in the peritoneal cavity* during dialysis therapy between scheduled fluid exchanges. The "exchange" refers to the process of *discarding used* dialysis solution and *instilling fresh* dialysis solution into the peritoneal cavity.

There are two types of peritoneal dialysis: (1) automated peritoneal dialysis (APD), and (2) continuous ambulatory peritoneal dialysis (CAPD). The fluids routinely in use include solutions of various concentrations of glucose and dextrin solution. In a 24-hour period, a peritoneal dialysis patient would typically utilize ~10L of dialysis fluids.

- APD is performed using a fluid cycling machine for instillation and drainage of the dialysis solution. The key dialysis component takes place at night with patients maintaining a dwell of fluid and/or additional fluid exchange(s) during the day.
- CAPD is performed by the patient using a gravity-based in-flow technique instead of a machine. Four solution-exchanges are typically used during a 24-hour period: three during the day and one at night. CAPD is an ongoing, permanent therapy, without respite ("24/7").

In CAPD, dextrin is used once a day, as described by Milner, for the long overnight dwell. One of ordinary skill in the art would be aware that, **only part of the daily total dialysis volume** would be dextrin because the dialysis fluid regimen includes dwell periods using other fluids (usually glucose-based) in addition to the single dwell period with dextrin.

Applicant now discusses the Dobbie abstract cited by the Examiner in the rejection of Claims 23 and 26-35 under 35 U.S.C. § 103(a).

Dobbie Abstract

The Dobbie abstract is a retrospective review of 900 uremic (i.e., kidney failure) patients. In particular, the Dobbie abstract provides a review of uremic patients before, during and after peritoneal dialysis treatment. The Dobbie abstract describes data that indicate a low occurrence of adhesions in patients treated **with peritoneal dialysis** as noted in lines 3-6.

At best, the Dobbie abstract suggests that the dialysis process of continuous peritoneal dialysis (CAPD) may be effective in reducing the incidence of adhesions in **peritoneal dialysis patients**. *See* lines 4-5. The Dobbie abstract suggests that chronic, repeated **replenishment** of fresh for waste-containing solutions could have affected the propensity to form adhesions **in CAPD patients**.

Applicant also respectfully submits that the Dobbie abstract does **not** "disclose **development of icodextrin** (glucose polymer) for use . . . post operatively in patients with a high risk of abdominal adhesions" as alleged in the Office Action on page 3, lines 24-28. The development of a solution which remains in the body cavity for at least 2 days as recited in Claim 23 of the instant application is not disclosed in the Dobbie abstract (see above). The Dobbie abstract fails to teach or suggest **any period of time or method** for an adhesion reduction effect. Instead, the Dobbie abstract considers the pathology of long-term peritoneal dialysis. One of ordinary skill in the art would be aware of the variable degree of diffuse peritoneal fibrosis in all patients who have been on long-term peritoneal dialysis.

Specifically, peritoneal dialysis-induced diffuse peritoneal fibrosis varies from opacification and "tanning" of the peritoneum (which may have a moderate detrimental effect on peritoneal transport kinetics) to a progressive, sclerosing encapsulating peritonitis which may lead to cessation of dialysis. The observational data discussed in the Dobbie abstract may suggest that, in the presence of this collateral damage to the peritoneal lining that occurs with prolonged dialysis, the **replenishment** of the peritoneal cavity fluid volume may be associated with a low occurrence of adhesion formation. In lines 12-14, the Dobbie abstract states that, in the context of **dialysis-related peritonitis**, "provided dialysis was **maintained**, accumulation of surface fibrin was minimized, while adhesions and fibrosis were rare" (emphasis added). There is no disclosure in the Dobbie abstract of a method to achieve

success in patients who do not display an induced diffuse peritoneal fibrosis, and wherein a peritoneal repair and remesothelialization would be an expected outcome. Thus, the Dobbie abstract does not direct one of ordinary skill in the art to a method of reducing adhesions in a body cavity that includes administering a composition including an aqueous formulation wherein the aqueous formulation is a solution that remains in the body cavity for at least 2 days.

The deficient teachings of the Dobbie abstract are not supplied by Milner for at least the reasons provided below.

Milner

The Milner patent discusses the composition and use of peritoneal dialysis solutions. As previously mentioned, peritoneal dialysis is a continuous therapeutic process, with clinical success achieved as a result of fluids being **instilled** and **withdrawn** from the peritoneal cavity on a **chronic-use basis**.

At column 11, lines 1-5, Milner discusses the method of peritoneal dialysis treatment with glucose polymers as follows:

The mode of use of the dialysis solutions according to the invention is similar to that of **known** dialysis solutions. The solution is infused into the peritoneum and allowed to remain there for a predetermined time, after which it is **withdrawn and replaced by a fresh solution**. (emphasis added).

At column 11, lines 17-26, Milner further states the following:

In favourable cases it is possible for peritoneal dialysis solutions of the present invention to be allowed usefully to remain in the peritoneum **for as long as eight hours**. The daily regimen for a patient suffering from chronic renal failure and being treated by continuous ambulatory peritoneal dialysis then involves three exchanges per day. Each infusion is of two litres in volume so the total infusion per day is six litres. The total amount of fluid **withdrawn per day** is 7.2 litres....(emphasis added).

In essence, Milner provides the following regarding a peritoneal dialysis solution:

- 1) The peritoneal dialysis solution is replaced throughout the day;
- 2) More fluid than is given per day is withdrawn per day and;
- 3) The maximum dwell period for a single infusion is 8-12 hours.

Applicant respectfully submits that the Office Action has selectively quoted from Milner. See Office Action page 4, lines 17-20. Milner clearly describes **repeated instillations** of a volume and **removals** of a larger total volume using a single day of

experimentation from a **chronic** treatment situation. It should be emphasized that the instant invention requires an instillation that is **not** removed as provided by Milner.

In view of the Dobbie abstract and Milner, one of ordinary skill in the art would be directed to a method characterized by removal and replacement of fluid several times per day to effect a reduction in adhesion occurrence. There is no teaching, in either the Dobbie abstract or Milner, of how reduction of adhesion formation could be achieved by a single instillate that remains in the body cavity for at least two days.

Lastly, Applicant directs the Examiner's attention to the Notice of Allowability issued by the United States Patent and Trademark Office (USPTO) on October 18, 2005. Under point 3 on pages 2-3, the Notice of Allowability indicates that Viegas (the closest prior art of record) and other prior art of record (which includes Milner) do not teach or fairly suggest a method of reducing the incidence of adhesions in a body cavity according to the recitations of Claim 23. The Dobbie abstract, which is directed exclusively to patients receiving peritoneal dialysis, and thus a **removal and replacement regimen**, does not teach or suggest a method to reduce the incidence of adhesions including allowing a solution to **remain** in a body cavity as recited in the pending claims. Applicant respectfully submits that the Dobbie abstract does not supply the missing recitations to render this statement inaccurate.

In summary, the Dobbie abstract does not motivate one of ordinary skill in the art to arrive at a method where a solution is allowed to remain in a body cavity where the Dobbie abstract is clearly directed to a solution that is removed from the body cavity. The cited references do not cure the deficiencies of the Dobbie abstract in reference to the present invention.

Accordingly, Applicant respectfully submits that Claims 23 and 26-35 are patentable over the cited references, and Applicant respectfully requests that the rejection of these claims under 35 U.S.C. § 103 be withdrawn for at least the reasons previously made of record and presented herein.

III. **New Claims**

Applicant has added new Claims 45-51. Support for these claims can be found in the specification and claims as originally filed, for example, page 4, lines 17-30 and Claims 29-31 and 34.

Applicant submits that, as noted above, the Dobbie abstract does not teach or suggest a method of reducing adhesions in a body cavity employing a solution wherein the solution is allowed to remain in the body cavity. Further, the Dobbie abstract does not teach or suggest a method of reducing adhesions in a body cavity employing a solution wherein (a) the aqueous formulation is a solution in the body cavity and remains in the body cavity for at least 2 days, (b) dextrin is applied to the body cavity in an amount of about 4 % weight to volume of the composition; and (c) the composition including the aqueous formulation is administered intraperitoneally. Accordingly, Applicant respectfully requests entry and allowance of new Claims 45-51.

Conclusion

In view of the foregoing amendments and remarks, Applicant respectfully requests that all outstanding rejections to the claims be withdrawn and that a Notice of Allowance be issued in due course.

Applicant respectfully requests an interview with the Examiner at the USPTO should there be any remaining significant issues preventing the allowance of the present application. In any event, any questions that the Examiner may have should be directed to the undersigned, who may be reached at (919) 854-1400.

Respectfully submitted,



Shawna Cannon Lemon
Registration No. 53,888

USPTO Customer No. 20792
Myers Bigel Sibley & Sajovec, P.A.
P. O. Box 37428, Raleigh, NC 27627
Telephone: (919) 854-1400
Facsimile: (919) 854-1401

CERTIFICATION OF TRANSMISSION UNDER 37 CFR § 1.8

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